REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claim 26 was objected to as being improperly multiple dependent. In response, Applicants have corrected the dependency of claim 26 to claim 1 only.

Claim 69 was rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants have amended claim 69 in a manner that Applicants believe addresses the Examiner's concerns and renders claim 69 clearly definite.

Claims 1, 3-5, 12, 15, 20, 23, 26, 28, 33 and 69 were rejected under 35 USC § 102(b) as being anticipated by Kamb, US 20030027214. In response, Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, if the Examiner relies on a theory of inherency as to any particular element, then the extrinsic evidence must make clear that such element is *necessarily* present in the thing described in the reference, and the presence of such element therein would be so recognized by persons skilled in the art. *In re Robertson,* 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, inherency is not established by probabilities or possibilities, and the mere fact that a property may result from a given circumstances is not sufficient; instead it must be shown that such property *necessarily* inheres in the thing described in the reference. *Id.* Kamb does not teach "lysates comprising a plurality of proteins expressed by the respective cells [populations(s)]," as required by the instant claims. Consequently, Kamb cannot anticipate the rejected claims.

Kamb describes generating a soluble lysate of one particular clone, which in turn corresponds to one individual polypeptide or one unique polypeptide of a polypeptide library (proteinaceous substrate obtained in an expression step). Alternatively each member of a non-proteinaceous substrate pool of interest is individually arrayed at a unique location [0031]. Obtained lysates are deposited on a solid support that is suitable for adhering a desired polypeptide from a polypeptide containing lysate [0032]. The product of step 1 to 3 is therefore a solid support comprising on its surface a plurality of measurement areas, which location may be tracked to identify the corresponding lysate, wherein each measurement area comprises one unique polypeptide (proteinaceous substrate) or non-proteinaceous substrate of interest. If an array is generated on a well-plate, each well produces a unique polypeptide [0052], with a corresponding unique array location that can be referenced throughout the ligand screening process [0054]. Once the measurement areas are produced a number of specific binding partners are applied and the substrate/ligand interactions can be quantified [0089] by measurement of fluorescence in a locally resolved manner [0092, 0093]. Please also note that in Kamb adhesion of unique peptide of step 3 is achieved selectively using adhesion moiety biotrx/GFP/streptavidin/complex, DHFR/GFP/methotrexate [0103], calmodulin/CBP or other [0107], whereby proteinaceous substrate is modified to incorporate biotrx or DHFR. When the library polypeptides are simply adhered to a solid support, the library polypeptide has to be separated from the other host cell polypeptides [0110].

This is to be opposed to the lysates comprising a plurality of proteins of step 1 in current claim 1 (or claim 2), which are to be analyzed simultaneously. The product of steps 1 to 3 of the

rejected claims is a measurement area comprising a plurality of proteins expressed by a cell population ("inverted assay architecture", instant specification, p. 4, ¶ 3). Deposition is performed directly on solid support or on an adhesion-promoting layer without modification or separation of the proteinaceous analytes.

In view of the foregoing, Applicants respectfully submit that Kamb does not anticipate the rejected claims. An early notice to that effect is earnestly solicited.

Claims 2, 6-8, 14 and 29 were rejected under 35 USC § 103(a) as being obvious over Kamb. In response, Applicants respectfully submit that Kamb does not make out a *prima facie* case of the obviousness of the rejected claims.

The Examiner concedes that Kamb does not teach providing lysates from more than one population of cells. However, the Examiner finds that providing a second population of cells in the array would have been obvious because the desirability of such simultaneous screening is well known in the art and is also discussed by Kamb in paragraph [0005].

In response, Applicants respectfully disagree that a person having ordinary skill in the art would, in fact, have been so motivated. Indeed, Applicants respectfully submit that such a person would not have had any motivation to modify the teaching of Kamb in immobilizing a plurality of proteins expressed by a cell population because he would have expected to lose the possibility to identify protein/ligand pair by tracing unique array location [0052]. Consequently, such a person would not, in fact, have been motivated to make the modifications in Kamb necessary to achieve the invention of the rejected claims.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and

withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 9 and 11 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Shen et al. ("Shen"), US 6,458,829. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Shen overcomes the above-noted deficiencies of Kamb. Indeed, Shen only mentions in-vitro assays for selection and screening of anti-inflammatory compounds and cellular assays for in-vitro study of inflammation reaction in general.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 10 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Gundersen et al. ("Gundersen"), US 20030129749. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Gundersen overcomes the above-noted deficiencies of Kamb. Indeed, Gundersen only describes comparison of diseased and healthy cell population is.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 13 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Oh et al. ("Oh"), US 5,863,742. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Oh overcomes the above-noted deficiencies of Kamb. Indeed, Oh only describes addition of an intracellular protein to the analyte of the cell lysate for control.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 16-19, 24 and 25 were rejected under 35 USC § 103(a) as being obvious over Eipel et al. ("Eipel"), US 6,737,024, in view of Kamb. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Eipel overcomes the above-noted deficiencies of Kamb. Indeed, although the considers the hydrophobic coating of Eipel and the adhesion-promoting layer of the rejected claims be equivalent, Applicants disagree.

The hydrophobic coating of Eipel prevents the measurement zone spreading into one another, providing a "wall" to chemically defined wells of µm-size, thereby solving the problem of increasing capillary forces in µm-sized wells. Reagents or cells are placed on the measurement points on the support surface and bring about reaction thereof. Proteins or nucleic acid can be present in adsorbed or in chemically bound form (col. 4, l. 59-col 5, l. 4). Further details on how

chemical binding may be achieved are not given.

The purpose of the adhesion-promoting layer of the present invention is to improve adhesion of the proteins contained in the deposited lysates in comparison to purely adsorptive immobilization on the surface of the support (p. 16, ¶ 3).

In other words the adhesion-promoting layer of the embodiments of the rejected claims enhance the chemical binding of proteins within measurement areas, whereas the hydrophobic coating of Eipel only defines the outer limits of measurement areas.

The hydrophobic coating of Eipel and the adhesion-promoting layer of rejected claims are, therefore, not equivalent. As binding proteins is not an issue of Eipel, persons having ordinary skill in the art would not have been motivated to combine Kamb and Eipel. And, had he done so, he would rather have been motivated to replace classic well-plates used by Kamb by chemically defined well-plates of Eipel in order to minimize volumes but certainly would not have been motivated to modify the immobilization of the proteinaceous analytes of Kamb.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 21 and 22 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Craig et al. ("Craig"), US 6,972,198. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Craig overcomes the above-noted deficiencies of Kamb. Indeed, Craig only describes an

immobilization assay wherein adhesion of one protein on the surface of a solid support is achieved using an adhesion moiety as described by Kamb [col. 19, l. 25-col. 20, l. 7]. Craig also teaches this concept of immobilized assay can be applied to measure the activities of multiple post-translational modification enzymes in a complex sample [Assay 6, col. 20, l. 11-16] that is to a plurality of proteins to be analyzed simultaneously. However the solution of Craig comprises a common peptide partner or a specific partner for each target protein immobilized on a solid support. The sample (e.g. the lysate) is then added to the immobilized array of specific binding partners [col. 20, l.23 to 26] allowing the separation of the proteins of interest from the rest of the lysate.

This is not the immobilized assay of the rejected claims wherein a plurality of proteins are deposited directly on solid support or on an adhesion-promoting layer without modification or separation of the proteinaceous analytes.

A person having ordinary skill in the art would not have been motivated to modify the method of Craig for a plurality of proteins as he would have lost selective binding of proteins of interest on the support.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claim 27 was rejected under 35 USC § 103(a) as being obvious over Kamb in view of Matson et al. ("Matson"), US 7,070,740. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be

anticipated, which, Applicants have explained above, is not proper. Nothing in Matson overcomes the above-noted deficiencies of Kamb. Indeed, Matson only teaches that well plates for assays can be used for trans- or epi-illumination reading using the architecture of Kamb.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 30-32 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Lackritz et al. ("Lackritz"), US 6,956,651. In response, Applicants respectfully submit that this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Lackritz overcomes the above-noted deficiencies of Kamb. Indeed, Lackritz teaches an array architecture wherein the support sensor is coated with a member of a binding pair (MBP), chosen because they interact exclusively with a selected target, analyte or molecule of a sample. When the support sensor is exposed to a sample that contains analyte molecules, they bind to the sensors surface via their specific interaction with MBP. Detection is achieved by comparison of the observed surface plasmon resonance shift with a stored calibration curve.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Claims 34-41 were rejected under 35 USC § 103(a) as being obvious over Kamb in view of Duveneck et al. ("Duveneck"), US 6,395,558. In response, Applicants respectfully submit that

this rejection was dependent on the propriety of the basis on which the Examiner found claim 1 to be anticipated, which, Applicants have explained above, is not proper. Nothing in Duveneck overcomes the above-noted deficiencies of Kamb. Indeed, Duveneck only discloses an optical wave guide on which the architecture also described by Kamb is allegedly applied.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has also been reconsidered and withdrawn is earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,

NORRIS MCLAUGHLIN & MARCUS, P.A.

By /Kurt G. Briscoe/

Kurt G. Briscoe
Attorney for Applicant(s)
Reg. No. 33,141
875 Third Avenue - 8th Floor
New York, New York 10022
Phone: (212) 808-0700
Fax: (212) 808-0844